

REMARKS/ARGUMENTS

I. Status of the Claims

After entry of this Response, claims 1-4, 6-18 are pending. Claims 1-4, 6-8 and 18 are currently presented. Claims 1-4, 6-8 and 18 are allowed. Claim 5 is cancelled. Claims 9-17 are withdrawn.

II. The Invention

The present invention relates to quinolones and compounds related to quinolones. One use of these quinolones and compounds thereof is for the inhibition of viruses, *e.g.*, HIV. The invention further relates to methods of making these compounds, methods of identifying the efficacy of these compounds, and methods of using these compounds to inhibit or prevent HIV infection and related disease states such as AIDS.

III. The Response to the Advisory Action

In a teleconference with Applicants' representatives on Tuesday, April 19, 2005, the Examiner noted that composition of matter claims 1-4, 6-8 and 18 are in condition for allowance. Since claims 9-17 are methods of using these compositions of matter, Applicants have requested the rejoinder of these claims. In a teleconference with Applicants' representatives on Friday, May 13, 2005, the Examiner indicated that these claims may be rejoined upon the presentation of biological data demonstrating the efficacy of the methods in claims 9-17. Although such biological data are not required for rejoining the claims, for purposes of expediting prosecution Applicants would like to present efficacy data and thus comply with the Examiner's wishes.

Applicants submit three Tables with this Response. Table 1 is a description of the virus employed in the biological testing assay. Vesicular stomatitis virus-glycoprotein ("VSV-g") pseudotyped HIV-1 luciferase reporter virus ("HIV-1 pseudovirions") was used in this assay. The viral vector RNA synthesized from the HIV-1 LTR:Luc plasmid possesses the *cis* RNA packaging signal (psi sequence) in addition to the luciferase reporter gene and the HIV-1 LTR. The supernatants of transfected producer cells contain HIV-1 pseudovirions

carrying only the luciferase gene in the viral genome. This HIV pseudovirion is commonly used in the industry for HIV inhibition assays.

The assay protocol is provided in Table 2. According to the protocol, HEK 293T cells (human cells) were seeded and provided conditions to ensure their growth and viability (steps 1 and 2). A compound of the invention was then added to the HEK 293T cell culture (step 3). In step 4, the HIV pseudovirion was added to the HEK 293T cell culture. Enough of the HIV pseudovirion was added in order to attain a ratio of one virus per HEK 293T cell, or a multiplicity of infection (MOI) of 1. After incubation for an additional 48 hours (step 5), viral activity was monitored by monitoring luciferase activity via plate reading of the fluorescent luciferase product on a CLIPRTM apparatus (step 6). By comparing the amount of fluorescence produced from this cell culture with a cell culture that did not receive the quinolone compound, the degree of viral inhibition caused by the presence of the quinolone compound was ascertained. EC50 data was generated by determining the quinolone concentration at which HIV activity was inhibited by 50%.

Table 3A-3O includes physical and biological assay data for the compounds of the invention. The biological data is located in the far right-hand column entitled "EC50 (μ M) (293 T)". The data in this column represents the quinolone concentration required to reduce HIV activity in Human Embryonic Kidney (HEK) 293T cells by 50%.

CONCLUSION

In view of the above, method claims 9-17 should be rejoined with the composition of matter claims. Allowance of claims 1-4, 6-18 is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

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PATENT

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